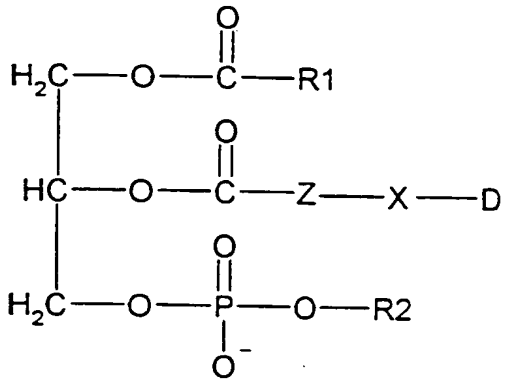
CLAIMS:

1. A prodrug of the general formula I:



Formula I

or a pharmaceutically acceptable salt thereof, wherein:

R1 is a saturated or unsaturated, straight-chain or branched, substituted or unsubstituted hydrocarbon chain having from 2 to 30 carbon atoms;

R2 is H or a phospholipid head group;

Z is saturated or unsaturated, straight-chain or branched, substituted or unsubstituted hydrocarbon chain having from 2 to 15 carbon atoms, which may include cyclic elements, and optionally is interrupted by one or more atoms selected from oxygen and sulfur atoms;

X is a direct covalent bond or selected from the group consisting of O, S, NH and C(O) groups; and

D is a residue of an anti-proliferative drug, methotrexate wherein the bound anti-proliferative drug residue is an inactive form of the drug which is selectively activated in cells and tissues with elevated phospholipase activity.

2. The prodrug according to claim 1, wherein the anti-proliferative drug is methotrexate or pharmaceutically acceptable derivatives thereof.

3. The prodrug according to claim 1, wherein the anti-proliferative drug is 2'-deoxy-5-fluorouridine and pharmaceutically acceptable derivatives thereof.

4. The prodrug according to claim 1, wherein an ester bond at position sn-2 of the phospholipid of the general formula I is cleaveable by a phospholipase.

5. The prodrug according to claim 4, wherein said phospholipase is phospholipase A_2 (PLA_2).

6. The prodrug according to claim 1, wherein R1 is a hydrocarbon chain having from 5 to 20 carbon atoms.

7. The prodrug according to claim 1, wherein R1 is a hydrocarbon chain having 15 or 17 carbon atoms.

8. The prodrug according to claim 1, wherein R2 is selected from the group consisting of choline, ethanolamine, inositol and serine.

9. The prodrug according to claim 1 selected from the group consisting of:

1-Stearoyl-2-[3-(α-MTX amido)-Propanoyl]-sn-Glycero-3-Phosphatidylcholine,

1-Stearoyl-2-[3-(γ-dodecylate-α-MTX amido)-Propanoyl]-sn-Glycero-3-Phosphatidylcholine,

1-Stearoyl-2-[4-(α-MTX amido)-Butanoyl]-sn-Glycero-3-Phosphatidylcholine,

1-Stearoyl-2-[6-(α-MTX amido)-Hexanoyl]-sn-Glycero-3-Phosphatidylcholine,

1-Stearoyl-2-[8-(α-MTX amido)-Octanoyl]-sn-Glycero-3-Phosphatidylcholine,

1-Stearoyl-2-[8-(γ-dodecylate-α-MTX amido)-Octanoyl]-sn-Glycero-3-Phosphatidylcholine,

1-Stearoyl-2-[3-(α-dodecylate-γ-MTX amido)-Propanoyl]-sn-Glycero-3-Phosphatidylcholine, and

1-stearoyl-2-[5"-(2''-deoxy-5'-fluorouridine-5"-)-3"',3"'–dimethyl] glutaroyl-1"'-sn-glycero-3-phosphatidylcholine

10. The prodrug according to claim 1 which is 1-Stearoyl-2-[3-(α-MTX amido)-Propanoyl]-sn-Glycero-3-Phosphatidylcholine.

11. The prodrug according to claim 1 which is 1-Stearoyl-2-[3-(α-dodecylate-γ-MTX amido)-Propanoyl]-sn-Glycero-3-Phosphatidylcholine.

12. A pharmaceutical composition comprising, as an active ingredient, a prodrug of the general formula I according to any one of claims 1 to 11, and a pharmaceutically acceptable carrier.

13. The pharmaceutical composition according to claim 12 further comprising an additional anti-neoplastic agent.

14. The pharmaceutical composition according to claim 12 or claim 13, which is suitable for oral, ocular, nasal, parenteral, topical or rectal administration.

15. The pharmaceutical composition according to claim 12 or claim 13, which is suitable for oral administration, intravenous administration or topical administration.

16. The pharmaceutical composition according to claim 12 or claim 13, in the form of solutions, suspensions, capsules, tablets, aerosols, gels, ointments or suppositories.

17. Use of a prodrug as defined in any one of claims 1 to 11 for the manufacture of a medicament.

18. A method for treatment of a disease or disorder related to an inflammatory condition comprising administering to a patient in need thereof a therapeutically effective amount of a pharmaceutical composition according to claim 12.

19. The method according to claim 18, wherein said disease or disorder related to an inflammatory condition is selected from the group consisting of granulomatous diseases, arthritis, rheumatoid arthritis, multiple sclerosis, systemic sclerosis, asthma, psoriasis, systemic lupus erythematosus, inflammatory bowel syndromes and migraines.

20. A method for treatment of a disease or disorder related to a degenerative or atrophic condition comprising administering to a patient in need thereof a therapeutically effective amount of a pharmaceutical composition according to claim 12.

21. The method according to claim 20, wherein said disease or disorder related to a degenerative or atrophic condition is a central or peripheral neurological disease or disorder.

22. The method according to claim 20, wherein said disease or disorder related to a degenerative or atrophic condition is selected from the group consisting of autoimmune, cerebrovascular and neurodegenerative diseases and disorders such as idiopathic dementia, vascular dementia, multi-infarct dementia, traumatic dementia, Alzheimer's disease, Pick's disease, Huntington's disease, dementia paralitica, Parkinson's disease, diabetic neuropathy, amyotrophic lateral sclerosis, ischemia of the optic nerve, age-related macular degeneration, stroke and trauma.

23. A method for treatment of a disease or disorder related to uncontrolled cell growth comprising administering to a patient in need thereof a therapeutically effective amount of a pharmaceutical composition according to claim 12.

24. The method according to claim 23, wherein said disease or disorder related to uncontrolled cell growth is a neoplastic growth.

25. The method according to claim 24 wherein said neoplastic growth is a primary or a secondary tumor.

26. The method according to claim 24 wherein said neoplastic growth is a drug-resistant tumor.

27. The method according to claim 24 wherein said neoplastic growth is a methotrexate-resistant tumor.

28. The method according to claim 24 wherein said neoplastic growth is a multidrug-resistant tumor.

29. The method according to claim 23, wherein said disease or disorder related to uncontrolled cell growth is selected from the group consisting of psoriasis, lymphocytic leukemia, myelogenous leukemia, Burkitt's lymphoma, non-Hodgkin's lymphomas, mycosis fungoides, osteosarcoma, hydatidiform mole, trophoblastic diseases such as chorioadenoma destruens and choriocarcinoma, and carcinomas of the head and neck, breast, liver, lung, colon, ovary, cervix, urinary, bladder, prostate, pancreas, skin, the gastrointestinal tract and the oropharyngeal areas.